



## Hepatitis B Vaccine Recombinant, Adjuvant (HEPLISAV-B)

Classification: Vaccines

### Description:

Hepatitis B is a liver infection caused by the Hepatitis B virus (HBV). HBV is transmitted when blood, semen, or another body fluid from a person infected with the Hepatitis B virus enters the body of someone who is not infected. This can happen through sexual contact; sharing needles, syringes, or other drug-injection equipment; or from mother to baby at birth. For some people, hepatitis B is an acute, or short-term, illness but for others, it can become a long-term, chronic infection. Risk for chronic infection is related to age at infection: approximately 90% of infected infants become chronically infected, compared with 2%–6% of adults. Chronic HBV can lead to serious health issues, like cirrhosis or liver cancer. <sup>1</sup> In 2016, a total of 3,218 cases of acute hepatitis B were reported to CDC. <sup>2</sup> The rate of new HBV infections has declined from 1990–2014. The decline has been greatest among children born since 1991, when routine vaccination of children was first recommended. Since 2014, there has been an increase in the rate of new HBV infections, which is likely due to increasing injection drug use. <sup>3</sup>

### Pharmacology:

All HBV vaccines in the US available in the US contain recombinant yeast-derived hepatitis B surface antigen (HBsAg), with an immunostimulatory adjuvant. While all other available hepatitis B vaccines use aluminum hydroxide as an adjuvant, Heplisav-B uses CpG as the adjuvant. This is thought to lead to the production of cytokines such as interleukin-12 and interferon- $\alpha$ . <sup>5, 7</sup>

### Indication:

Heplisav-B is indicated for prevention of infection caused by all known subtypes of hepatitis B virus. It is approved for use in adults 18 years of age or older. <sup>6</sup>

### Dosage and administration:

Two doses, 0.5 ml each, one month (at least 4 weeks) apart. <sup>6,7</sup>

Administer HEPLISAV-B by intramuscular injection in the deltoid region.

Heplisav-B is a clear to slightly opalescent, colorless to slightly yellow solution; do not administer if particulate matter or discoloration is present.

2-dose Heplisav-B vaccine series only applies when both doses consist of HepB-CpG, administered at least 4 weeks apart.

A series consisting of a combination of one dose of HepB-CpG and a vaccination from a different manufacture (HepB-aluminum) should adhere to the following:

- Adhere to the 3 dose schedule with minimum intervals of 4 weeks between doses 1 and 2, 8 weeks between doses 2 and 3, and 16 weeks between doses 1 and 3. However, if HepB-CpG is substituted for dose 2 of Hep-B Alum, a provider has the option of administering the next dose of HepB-CpB a minimum of 4 weeks from the previous dose for a complete series.<sup>7</sup>

### **Contraindications:**

Do not administer HEPLISAV-B to individuals with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of HEPLISAV-B, including yeast.<sup>6,7</sup>

### **Precautions**

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of HEPLISAV-B. <sup>6</sup>.

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to HEPLISAV-B. <sup>6</sup>

Hepatitis B has a long incubation period. HEPLISAV-B may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration. <sup>6</sup>

### **Interactions:**

Use with immune globulins. There are no data to assess the commodities use of Heplisav-B with immune globulin. When concomitant administration of Heplisav-B and immune globulin are required, they should be given with different syringes at different injection sites.<sup>6</sup>

Interference with laboratory values: Serum HBsAg may not have diagnostic value within 28 days after receipt of Heplisav-B.<sup>6</sup>

Use in special Populations:

Pregnancy: There is a pregnancy exposur registry that monitors pregnancy outcome in women exposed to Heplisav-B. There are no clinical studies of Heplisav-B in pregnant women.<sup>6</sup> Until safety data is available for Heplisav-B, providers should continue to vaccinate pregnant women needing Hepatitis B Vaccine with Hep-B-Alum (ENGERIX-B® or RECOMBIVAX HB®) <sup>7</sup>.

Lactation: It is not known whether Heplisav-B is excreted in human milk. Data are not available to assess the effects of Heplisv-B on the breast feeding infant or on milk production/excretion. <sup>6</sup>

Safety and efficacy of Heplisav-B have not been established in adults on hemodialysis. <sup>6</sup>

Adverse Effects:

The most common adverse effects of Heplisav-B in clinical trials were:

Injection site pain (23% to 39%)

Fatigue (11%-17%), and headaches (8%-17%). <sup>5</sup>

Cost:

Heplisav-B AWP cost per vial \$138.00

AWP Cost per series \$276.00

Sold as box of 5 doses.

Enerix-B AWP Cost per vial \$68.70

AWP Cost per series \$206.10

Sold as box of 10 doses.

Efficacy:

The immunogenicity of the new vaccine was evaluated in three randomized, observer-blind, studies that compared the rates of seroprotection after two doses of Heplisav-B at one and 4 weeks, to the other after 3 doses of Engerix-B given at 0, 2, and 6 months. Separation rates were significantly higher with Heplisav-B than with Engerix-B .

### Conclusion:

The Advisory Committee on Immunization Practices (ACIP) has approved the recommendation for Heplisav-B vaccine to be an option for previously unvaccinated or incompletely vaccinated persons, including adults 18 years and older who have specific risk, or lack a risk factor but want protection.<sup>7</sup> In clinical trials, two doses of Heplisav-B were more immunogenic than three doses of an older hepatitis B vaccine (Engerix-B), but Heplisav-B caused more injection site reactions. The rate of serious adverse effects with the two vaccines were similar, but long term safety of Heplisav-B remains to be established. <sup>5</sup>

Recommendation: Add to Formulary.

### References:

1. The Center for Disease Control and Prevention, Viral Hepatitis, Hepatitis B. CDC Hepatitis B information, Q&As for Health Professionals.
2. CDC. Viral Hepatitis Surveillance–United States, 2016. 2018.
3. Harris AM, Iqbal K, Schillie S, Britton J, Kainer MA, Tressler S, et al. Increases in Acute Hepatitis B Virus Infections – Kentucky, Tennessee, and West Virginia, 2006-2013. MMWR Morb Mortal Wkly Rep. 2016;65(3):47-50.
4. CDC, Hepatitis B questions and answers for healthcare professionals. What are the hepatitis B vaccines licensed for use in the United States?
5. From the Medical letter on drugs and therapeutics. A Two Dose Hepatitis B Vaccine for Adults, (Heplisav-B) JAMMA, February 17, 2018. Volume 319, numbers 8.
6. Heplisav-B Package insert, Dyanavax .
7. Advisory Committee on Immunization Practices (ACIP) recommendations. Heplisav-B (HepB-Cp-GpG) Vaccine.

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